

**Amendments to the Claims:**

This listing of claims will replace all prior versions and listings of claims in the application:

**Listing of Claims:**

1-50. (cancelled)

51. (new) A method for screening a plurality of compounds so as to identify at least one compound exhibiting cognitive enhancing activity, comprising:

- a) determining *in vitro* efficacy and EC<sub>50</sub> values for each compound at an  $\alpha_1\beta_2\gamma_2$  or an  $\alpha_5\beta_3\gamma_2$  GABA<sub>A</sub> subtype receptor;
- b) determining an *in vitro* efficacy value for each compound at a GABA<sub>A</sub> receptor comprising an  $\alpha_2$  or  $\alpha_3$  subunit; and
- c) identifying as exhibiting cognitive enhancing activity a compound having: an EC<sub>50</sub> value determined in a) of less than about 200nM, an efficacy value determined in a) of less than about -5%, and an efficacy value determined in b) of greater than about 5%.

52. (new) The method of Claim 51 wherein the EC<sub>50</sub> measured in step a) is less than 150 nM.

53. (new) The method of Claim 52 wherein the *in vitro* efficacy measured at said  $\alpha_1\beta_2\gamma_2$  GABA<sub>A</sub> subtype receptor or said  $\alpha_5\beta_3\gamma_2$  GABA<sub>A</sub> subtype receptor is less than -10%.

54. (new) The method of Claim 53 wherein the *in vitro* efficacy measured at said GABA<sub>A</sub> receptor comprised of said  $\alpha_2$  subunit or said  $\alpha_3$  subunit is greater than 10%.

55. (new) The method of Claim 51 wherein the *in vitro* efficacy measured at said  $\alpha_1\beta_2\gamma_2$  GABA<sub>A</sub> subtype receptor or said  $\alpha_5\beta_3\gamma_2$  GABA<sub>A</sub> subtype receptor is less than -10%.

56. (new) The method of Claim 55 wherein the *in vitro* efficacy measured at said GABA<sub>A</sub> receptor comprised of said  $\alpha_2$  or said  $\alpha_3$  subunit is greater than 10%.

57. (new) The method of Claim 51 wherein the GABA<sub>A</sub> receptor comprised of said  $\alpha_2$  subunit is an  $\alpha_2\beta_3\gamma_2$  GABA<sub>A</sub> receptor or the GABA<sub>A</sub> receptor comprised of said  $\alpha_3$  subunit is an  $\alpha_3\beta_3\gamma_2$  GABA<sub>A</sub> receptor.

58. (new) A method for screening compounds for cognitive enhancing activity, comprising:

- a) selecting compounds having a binding affinity less than 100 nM at any GABA<sub>A</sub> receptor;
- b) determining *in vitro* efficacy and EC<sub>50</sub> values for each selected compound at an  $\alpha_1\beta_2\gamma_2$  or  $\alpha_5\beta_3\gamma_2$  GABA<sub>A</sub> subtype receptor;

- c) determining *in vitro* efficacy and EC<sub>50</sub> values for each selected compound at a GABA<sub>A</sub> receptor comprised of an  $\alpha_2$  or  $\alpha_3$  subunit; and
- d) identifying as having cognitive enhancing activity any compound having an EC<sub>50</sub> value determined in b) of less than 200nM and an efficacy value measured in b) of less than -5%, and an efficacy value measured in c) of greater than 5%.

59. (new) A method for screening a plurality of compounds for cognitive enhancing activity, comprising:

- a) determining *in vitro* efficacy and EC<sub>50</sub> values for each compound at  $\alpha_1\beta_2\gamma_2$  or  $\alpha_5\beta_3\gamma_2$  GABA<sub>A</sub> receptors;
- b) determining *in vitro* efficacy for each compound at a GABA<sub>A</sub> receptor comprised of an  $\alpha_2$  or  $\alpha_3$  subunit;
- c) determining the *in vivo* effect of each compound in an animal model for measuring cognitive enhancement;
- d) determining the *in vivo* effects of each compound in an animal model for proconvulsant activity by measuring a seizure threshold in the presence of a seizure inducing compound or in an animal model that predicts anxiogenic effects; and
- e) identifying a cognitive enhancing compound as a compound having cognitive enhancing properties when the EC<sub>50</sub> measured in step a) is less than 200nM and the efficacy measured in step a) is less than -5% and the efficacy measured in step b) is greater than 5% and said compound produces a statistically significant ( $p < 0.05$ ) positive effect in the animal model indicative of cognitive enhancement and said compound does not produce an effect in the animal model predictive of

proconvulsant activity of more than a 25% decrease in the seizure threshold in the presence of the seizure inducing drug, or does not produce a change that is statistically significant in said model, or the compound does not produce a statistically significant effect in the animal model that predicts anxiogenic effects.

60. (new) A method for screening compounds for cognitive enhancing properties, comprising:

- a) selecting compounds having binding affinities of less than 100 nM at any GABA<sub>A</sub> receptor;
- b) measuring the *in vitro* efficacy of each compound at an  $\alpha_1\beta_2\gamma_2$  or  $\alpha_5\beta_3\gamma_2$  GABA<sub>A</sub> receptor;
- c) measuring the *in vitro* efficacy of each compound at a GABA<sub>A</sub> receptor comprised of an  $\alpha_2$  or  $\alpha_3$  subunit;
- d) measuring the *in vivo* effect of each compound in an animal model predictive of cognitive enhancement;
- e) measuring the *in vivo* side effects of each compound in an animal model that predicts proconvulsant activity by measuring a seizure threshold in the presence of a seizure inducing compound or measuring the *in vivo* side effects of each compound in an animal model that predicts anxiogenic effects; and
- f) identifying as a cognitive enhancing compound a particular compound for which the EC<sub>50</sub> measured in step b) is less than 200nM and the efficacy measured in step b) is less than -5% and the efficacy measured in step c) is greater than 5% and said particular compound produces a statistically significant (p < 0.05) positive effect in the animal model indicative

of cognitive enhancement and said particular compound does not produce an effect in the animal model predictive of proconvulsant activity of more than a 25% decrease in the seizure threshold in the presence of the seizure inducing drug, or does not produce a change that is statistically significant in said model, or said particular compound does not produce a statistically significant effect in the animal model that predicts anxiogenic effects.

61. (new) A method for screening a plurality of compounds so as to identify at least one compound exhibiting cognitive enhancing activity, comprising:

- a) determining *in vitro* efficacy and EC<sub>50</sub> values for each compound at an  $\alpha_1\beta_2\gamma_2$  and an  $\alpha_5\beta_3\gamma_2$  GABA<sub>A</sub> subtype receptor;
- b) determining an *in vitro* efficacy value for each compound at a GABA<sub>A</sub> receptor comprising an  $\alpha_2$  or  $\alpha_3$  subunit; and
- c) identifying as exhibiting cognitive enhancing activity a compound having: EC<sub>50</sub> values determined in a) of less than about 200nM at each subtype receptor, efficacy values determined in a) of less than about -5% at each subtype receptor, and an efficacy value determined in b) of greater than about 5%.

62. (new) The method of Claim 61 wherein the EC<sub>50</sub> values measured in step a) are less than 150 nM at each subtype receptor.

63. (new) The method of Claim 62 wherein the *in vitro* efficacy values measured in step a) are less than -10% at each subtype receptor.

64. (new) The method of Claim 63 wherein the *in vitro* efficacy measured at said GABA<sub>A</sub> receptor comprised of said  $\alpha_2$  subunit or said  $\alpha_3$  subunit is greater than 10%.

65. (new) The method of Claim 61 wherein the *in vitro* efficacy values measured in step a) are less than -10% at each subtype receptor.

66. (new) The method of Claim 65 wherein the *in vitro* efficacy measured at said GABA<sub>A</sub> receptor comprised of said  $\alpha_2$  or said  $\alpha_3$  subunit is greater than 10%.

67. (new) The method of Claim 61 wherein the GABA<sub>A</sub> receptor comprised of said  $\alpha_2$  subunit is an  $\alpha_2\beta_3\gamma_2$  GABA<sub>A</sub> receptor or the GABA<sub>A</sub> receptor comprised of said  $\alpha_3$  subunit is an  $\alpha_3\beta_3\gamma_2$  GABA<sub>A</sub> receptor.

68. (new) A method for screening a plurality of compounds so as to identify at least one compound exhibiting cognitive enhancing activity, comprising:

- a) determining *in vitro* efficacy and EC<sub>50</sub> values for each compound at an  $\alpha_1\beta_2\gamma_2$  and an  $\alpha_5\beta_3\gamma_2$  GABA<sub>A</sub> subtype receptor;
- b) determining an *in vitro* efficacy value for each compound at a GABA<sub>A</sub> receptor comprising an  $\alpha_2$  or  $\alpha_3$  subunit; and

c) identifying as exhibiting cognitive enhancing activity a compound having: EC<sub>50</sub> values determined in a) of less than about 200nM at each subtype receptor, an efficacy value determined in a) of less than about -10% at the  $\alpha_5\beta_3\gamma_2$  GABA<sub>A</sub> subtype receptor, an efficacy value determined in a) of greater than about 10% at the  $\alpha_1\beta_2\gamma_2$  GABA<sub>A</sub> subtype receptor, and an efficacy value determined in b) of greater than about 5%.

69. (new) The method of Claim 68 wherein the EC<sub>50</sub> values measured in step a) are less than 150 nM at each subtype receptor.

70. (new) The method of Claim 68 wherein the *in vitro* efficacy measured at said GABA<sub>A</sub> receptor comprised of said  $\alpha_2$  subunit or said  $\alpha_3$  subunit is greater than 10%.

71. (new) The method of Claim 68 wherein the GABA<sub>A</sub> receptor comprised of said  $\alpha_2$  subunit is an  $\alpha_2\beta_3\gamma_2$  GABA<sub>A</sub> receptor or the GABA<sub>A</sub> receptor comprised of said  $\alpha_3$  subunit is an  $\alpha_3\beta_3\gamma_2$  GABA<sub>A</sub> receptor.